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1994-1995 INFLUENZA SEASON: CANADIAN LABORATORY DIAGNOSES AND STRAIN CHARACTERIZATION

Introduction

In collaboration with the World Health Organization (WHO) international collaborating laboratories, provincial laboratories and other Canadian hospital and university-based virus laboratories, the Laboratory Centre for Disease Control (LCDC) conducts national surveillance on human influenza viruses. This surveillance monitors influenza activity, detects and describes antigenic changes in the circulating strains of influenza virus in Canada, and estimates, through periodic serosurveys, susceptibility to currently circulating and emerging strains. Canadian influenza surveillance information and actual representative strains are then shared with the WHO's collaborating centres for influenza to contribute to global influenza monitoring.

Influenza Activity

In general, the season in Canada began late in 1994 and continued into June, 1995. In addition, at least one influenza isolate has been reported in each month from July to September, 1995.

The data in Figure 1 indicate the number and month of laboratory-confirmed influenza virus isolations, detections and serodiagnoses reported from 26 of the 38 laboratories who contribute to the Canadian Virus Reporting (CVR) program, a surveillance program covering all laboratory-diagnosed viral diseases. There were 280 reports of influenza B from October through June, the largest number (69) occurring in April. Eight hundred and sixty laboratory reports of influenza A and influenza A subtypes were received from November through July; the peak number of reports (354) occurred in March.

Strain Characterization

Table 1 indicates the provincial source and identity of submitted isolates strain typed at LCDC, while Figure 2 shows the change in the predominating influenza A(H3N2) strains as the season progressed. A/Beijing/32/92-like strains were most prominent in February. A/Shangdong/09/93-like strains predominated in the March peak season and an increasing number of A/Johannesburg/33/94-like strains were typed in the late season from April to June, 1995.

Although A/Taiwan/01/86(H1N1) and A/Texas/36/91 are closely related, at least three of the nine strains identified late in the season as A/Texas/36/91-like (Table 1) were antigenically more closely related to A/Taiwan/01/86.

The majority of influenza B isolates were antigenically distinguishable from the B/Panama/45/90 strain in the 1994-1995 vaccine and most closely resembled B/Quindao/102/91 (Table 1) (Figure 3). B/Quindao/102/91 is closely related to B/Beijing/184/93, which is the WHO recommended influenza B component of the 1995-1996 influenza vaccine⁽¹⁾. However, the actual strain used by North American vaccine manufacturers is B/Harbin/07/94 because of its growth properties. The strains B/Beijing/184/93 and B/Harbin/07/94 are antigenically indistinguishable⁽²⁾. The first four strains that were most like B/Beijing/184/93 and B/Harbin/07/94 were submitted in June, 1995 (Figure 3).

Global Picture and Vaccine

Globally, influenza A(H3N2), A(H1N1), and B viruses also continued to circulate⁽¹⁾. Many recent isolates of influenza A(H3N2) viruses isolated from outbreaks or sporadic cases were antigenically distinguishable from the 1994-1995 vaccine strain A/Shangdong/09/93 and were similar to the recent reference strain A/Johannesburg/33/94⁽¹⁾.

Table 1
LCDC strain characterization completed on influenza isolates in Canada submitted from 1 December, 1994 to 21 July, 1995

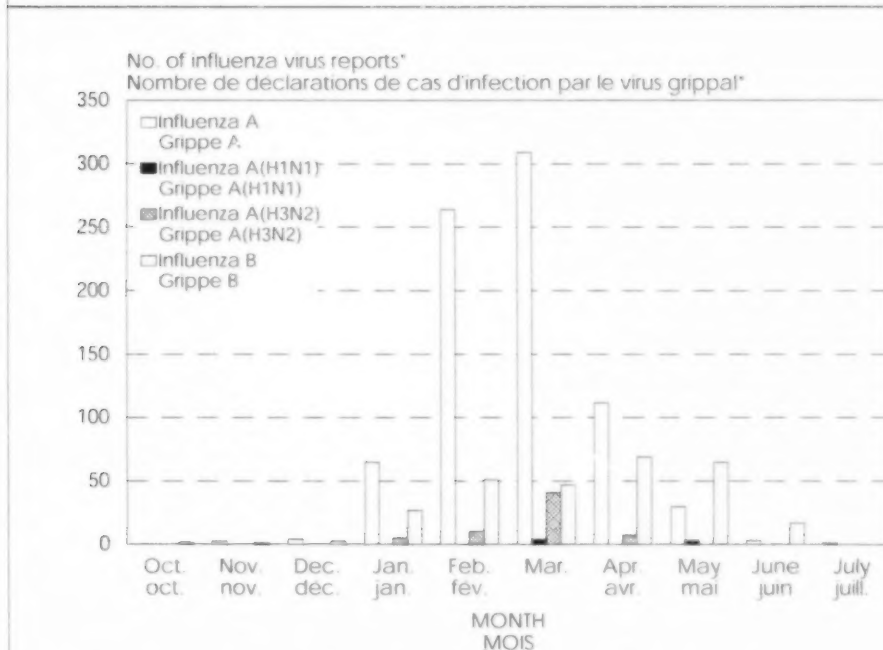
INFLUENZA	PROVINCE										TOTAL
	NFLD	PEI	NS	NB	QUE	ONT.	MAN.	SASK.	ALTA	BC	
TYPE A (H1N1)											
A/Texas/36/91-like				1				4	4		9
TYPE A (H3N2)											
A/Beijing/32/92-like					7	5	1	5	7	5	30
A/Shangdong/09/93-like			6	3	9	21	2	1	1		46
*A/Johannesburg/33/94-like	1		4	1	11	2	3			5	27
TOTAL A	1		10	5	27	28	6	13	12	10	112
TYPE B											
**B/Quindao/102/91-like				4	22	8	7	6	5	5	7
***B/Beijing/184/93-like					2						2
TOTAL B				4	24	8	7	6	5	5	59
TOTAL	1		10	9	47	36	13	19	17	15	171

* A/Johannesburg/33/94-like virus is the influenza A(H3N2) vaccine component in the 1995-1996 influenza vaccine⁽¹⁾.

** In hemmagglutination inhibition tests with rooster antisera, B/Quindao/102/91 appears to be more closely related to B/Beijing/184/93 than to B/Panama/45/90, which was the influenza B component of the 1994-1995 vaccine.

*** B/Beijing/184/93 is the recommended influenza B component of the influenza vaccine for 1995-1996⁽¹⁾.

Figure 1
Laboratory Evidence of Human Influenza Virus Infections in Canada, 1994-1995 Season



* From data available 22 August, 1995 — Canadian Virus Reporting Program, isolation, detection and serology

Influenza B viruses circulated widely and, just as in Canada, the majority of strains were antigenically distinguishable from the B/Panama/45/90 strain in the 1994-1995 vaccine and more closely resembled the recent reference strains B/Beijing/184/93 and B/Harbin/07/94⁽¹⁾.

Influenza A(H1N1) isolates were closely related antigenically to the current vaccine component⁽¹⁾.

Vaccines containing A/Shangdong/09/93(H3N2)-like viruses or B/Panama/45/90-like viruses induced protective hemagglutination-inhibiting antibody responses to A/Johannesburg/33/94-like and B/Beijing/184/93(H3N2)-like strains, respectively, at a lower frequency or lower geometric mean titre than to the vaccine viruses⁽¹⁾.

NACI, therefore, recommended⁽³⁾ that the trivalent influenza vaccine for the 1995-1996 season contain:

- an A/Johannesburg/33/94 (H3N2)-like strain,
- an A/Texas/36/91(H1N1)-like strain, and
- a B/Beijing/184/93-like strain.

Discussion

Antigenic drift in influenza A strains means that influenza strains with new coat proteins are continually emerging, and in the past season there was a rapid succession of distinguishable (H3N2) strains (Figure 2). The season began with a wave of A/Beijing/32/92-like strains (the 1993-1994 vaccine component), then A/Shangdong/09/93 (the 1994-1995 vaccine component) predominated, and finally in the late season, A/Johannesburg/33/94-like strains (1995-1996 vaccine component) were seen almost exclusively.

Note that in the late season the relative numbers of influenza B reports increased (Figure 1) and B/Beijing/184/93 and

Figure 2
LCDC Antigenic Characterization Completed on Influenza A(H3N2) Virus Isolates by Month of Submission from 1 December, 1994 to 30 June, 1995

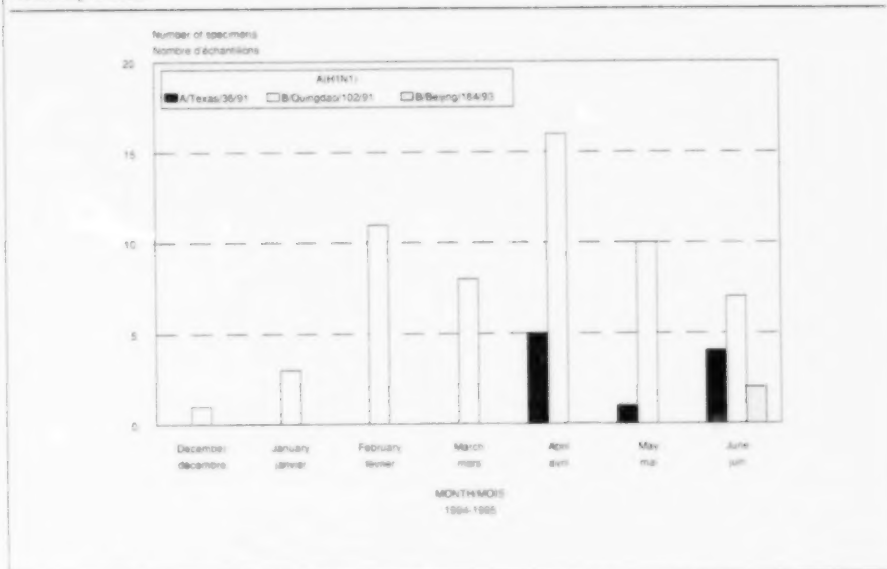
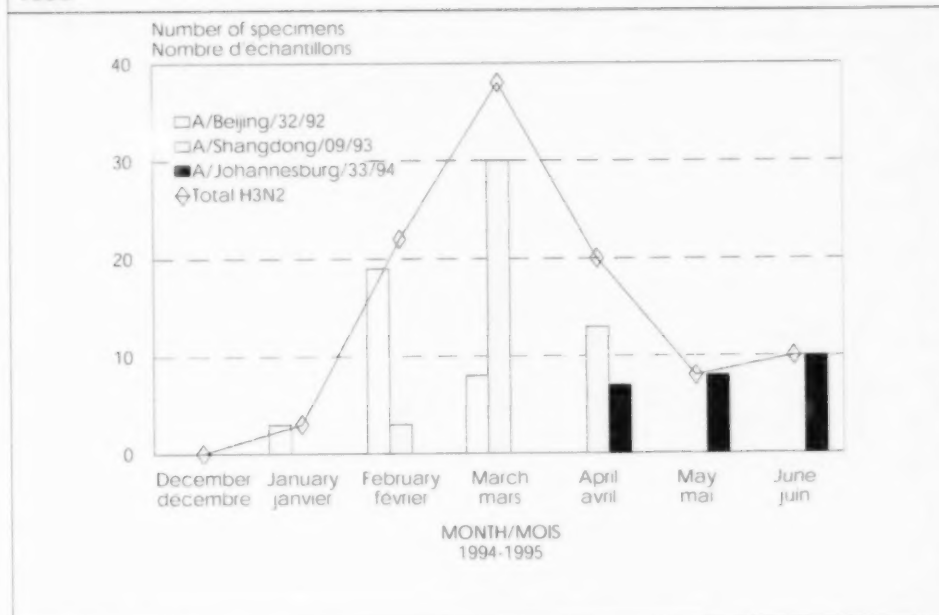


Figure 3
LCDC Antigenic Characterization Completed on Influenza B and A(H1N1) Virus Isolates by Month of Submission from 1 December, 1994 to 30 June, 1995



B/Harbin/07/94-like viruses were identified in June. Moreover, influenza A(H1N1) viruses were also present relatively late in the season (Figure 3).

Since antibody levels gradually decrease in the several months following influenza immunization and drifted variants of influenza A and B were encountered at the end of the 1994-1995 season, vaccination protection against this late season activity may have been less than optimal.

However, the strains that predominate in late season one year are often considered to be suggestive of the strains that will be prominent in the next season. Since immunization is the best protection against influenza, it is encouraging that the vaccine formulation for this coming season is well matched to the strains that were identified at the end of the 1994-1995 influenza season and likely to be common this winter.

Acknowledgements

The collaboration of laboratories in the CVR program and of provincial and hospital laboratories who forwarded early and representative isolates of influenza virus is a vital part of influenza surveillance in Canada.

Influenza virus isolates were submitted from the following centres:

British Columbia Centre for Disease Control, Virology Services, Vancouver, BC;

Provincial Laboratory of Public Health for Southern Alberta, Calgary, Alberta;

Provincial Laboratory of Public Health for Northern Alberta, Edmonton, Alberta;

Saskatchewan Public Health Laboratory, Laboratory and Disease Control Services Branch, Regina, Saskatchewan;

Cadham Provincial Laboratory, Winnipeg, Manitoba;

Regional Public Health Laboratory, Laboratory Services Branch, Virus Laboratory, Toronto, Ontario;

Laboratoire de santé publique du Québec, Sainte-Anne-de-Bellevue, Québec;

Laboratoire régional de virologie de l'Université Laval, Ste-Foy, Québec;

Hôpital G.L. Dumont, Moncton, New Brunswick;

Victoria General Hospital, Halifax, Nova Scotia;

Provincial Public Health Laboratory, St. John's, Newfoundland.

Carol Murano of LCDC conducted the influenza strain typing.

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Source: JM Weber, PhD, SCM (CCM). *Surveillance, Influenza and Viral Exanthemata, National Laboratory for Special Pathogens, Bureau of Microbiology, LCDC, Ottawa, Ontario.*

DENGUE FEVER IN CANADA

The incidence of dengue fever, a mosquito-transmitted viral illness, is rising in areas commonly frequented by Canadian tourists. There has been a marked increase in the number of cases over the past decade, especially in tropical and subtropical areas of Central and South America^{1,2,3}.

As of the beginning of September, there have been five cases of dengue fever diagnosed by the Laboratory Centre for Disease Control (LCDC) in Canadian travellers this year. These represent imported cases of infection since the vector for this illness, the *Aedes* mosquito, is not present in Canada. On average there are 10 cases of dengue fever reported to LCDC annually. It is important to note that underreporting of this infection occurs due to the fact that it often presents as a transient flu-like illness, for which medical advice may not be sought or for which serologic testing may not be carried out. Moreover, at this time dengue fever is not a reportable disease in Canada.

The following is a report of the recent cases reported to Quarantine Health Services at LCDC.

In August, a 72-year-old gentleman, originally from Haiti, presented to a Trois-Rivières hospital with dengue hemorrhagic fever, grade 1⁽⁴⁾. He was a diabetic but otherwise in good health. He had been living in New York since 1948, returned to Haiti from 3 to 8 August, 1995, and then proceeded to Quebec on 9 August. On 11 August, he experienced onset of a severe illness with high fever, chills, dizziness, nausea and anorexia. He also complained of arthralgias, particularly in his knees and lumbosacral area. By 13 August he sought medical attention. At that time, he had a temperature of 39°C and a pulse rate of 64 but was not toxic or in shock and his physical exam was otherwise unremarkable.

Blood cultures, malaria smear and chest x-ray were negative. Liver enzymes were elevated at twice the normal value. There was evidence of hemoconcentration with a hemoglobin of 172 g/L. He

also had thrombocytopenia, with a platelet count of $124 \times 10^9/L$, which reached a nadir of $17 \times 10^9/L$ on 15 August, and had increased to $74 \times 10^9/L$ 3 days later. His white blood cell count remained within normal limits; however, he had increased atypical lymphocytes, in keeping with a viral illness. On 15 August, his temperature returned to normal and his condition improved. He returned to New York on 18 August. Dengue serology, done on blood taken on 16 August, was positive for IgM at a titre ≥ 320 , confirming the diagnosis.

A total of 500 Canadian military personnel were deployed to the Port au Prince area of Haiti between March and September, 1995. They remained confined to camp until May, after that time they were permitted to spend more time in the local community, with the increased risk of exposure to the peridomestic *Aedes* mosquitoes.

Since June there have been 22 suspected cases of dengue fever in this military group, with three serologic confirmations to date.

One member required evacuation from Haiti to Miami due to thrombocytopenia. He presented with fever, severe myalgias and thrombocytopenia. He did not have shock at any time during his illness. When he was transferred on 14 July, his platelet count was $40 \times 10^9/L$; he required platelet transfusion once his count reached $15 \times 10^9/L$. He did not have any bleeding complications; however, bruising was noted at his intravenous site. This gentleman had dengue hemorrhagic fever, grade 1⁽⁴⁾.

A second member presented on 2 September with suspected dengue hemorrhagic fever, grade 1⁽⁴⁾, just 24 hours after finishing his tour in Haiti. He was in Montreal when he had the onset of fever, severe myalgias and headache. At the time he presented to a local hospital, he was noted to have thrombocytopenia, with his platelet count reaching a low of $13 \times 10^9/L$. Malaria smears were negative. He was treated conservatively and discharged from

hospital after 10 days. Confirmatory serology is pending. He was also noted to have a liver enzyme elevation five times the normal values.

These cases emphasize the risk to Canadians travelling in the Americas. The best "treatment" for dengue fever is prevention by avoiding the bite of the *Aedes* mosquito. Otherwise, supportive therapy is indicated, with close monitoring of the platelet count. Obviously malaria should be ruled out in any patient who has recently returned from the tropics with onset of fever and a flu-like illness. Unfortunately, the definitive diagnosis of dengue fever requires acute and convalescent serology.

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Source: Maj A McCarthy, MD, FRCP(C), DTM&H, Medical Advisor, Quarantine Health Services, LCDC, LCdr D Carpenter, MD, Directorate of Health Prevention and Promotion, Department of National Defence, Ottawa; M Goyette, MD, Chef du Service de microbiologie-infectiologie, Centre Hospitalier Saint-Joseph, Trois-Rivières, DT Nguyen, MD, FRCP(C), Internal Medicine, Hôpital Maisonneuve-Rosemont, Montréal, Québec.

Editorial Comment

The global increase in dengue activity noted by the authors of the above report has been associated with a worrying increase in the incidence of the disease in the Americas. While observed in this hemisphere for many years, dengue was not historically considered a major problem. Extensive programs designed to eradicate the principle vector for dengue and yellow fever, *Aedes aegypti*, from the Americas were not totally successful. The distribution of the mosquito has increased significantly during the past 20 years and the reinfestation of areas of the Americas has

been associated with increased spread of dengue viruses⁽¹⁾. This expansion of dengue activity has also been accompanied by an emergence of the more serious complications of infection, including dengue hemorrhagic fever⁽²⁾.

Currently, there is an expanding epidemic of the disease in Central America, Mexico and parts of the Caribbean basin. Nations in the affected areas are actively increasing mosquito control programs and are taking steps to improve the clinical management of severe cases of the disease to reduce mortality.

While the risks for international travellers remain low, infection can be observed in those returning from endemic areas⁽³⁾. Provisional figures for this calendar year indicate an increase in confirmed and suspected cases reported in travellers returning to Canada (H. Artsob, National Laboratory for Special Pathogens, LCDC: personal communication, 1995). The majority of these cases continue to be in travellers returning from Asia but, as noted in the above report, travellers to Central America and the Caribbean are also at risk of infection. Precautions to avoid contact with mosquitoes remain the primary intervention strategy for travellers to endemic areas.

An information package on dengue fever and dengue hemorrhagic fever/shock syndrome is available for physicians upon request by mail, or may be accessed through the LCDC's FAXlink service. FAXlink can be accessed 24 hours a day from the telephone on any fax machine, by dialing (613) 941-3900. This and other information on travel health is also available electronically through the Health Protection Branch Bulletin Board System or via the World Wide Web (<http://hpb.hwc1.8400>).

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International Notes

DENGUE IN THE AMERICAS

Dengue has emerged as an ongoing public health problem in many countries in the American tropics. During the last 10 years, five countries in South America have experienced epidemics following an absence of over 50 years. In 1995, 16 countries in the American Region had reported confirmed cases of dengue hemorrhagic fever (DHF).

Increased dengue activity has been reported by several Central American countries, and DHF has been reported in five of them. By 26 September, 1995, the Dominican Republic had reported 31 cases of DHF, El Salvador 114 cases (4 deaths), Honduras 15 cases (3 deaths), Nicaragua 338 cases (2 deaths), and Panama 2 cases (1 death). The Government of El Salvador has declared a state of national emergency. Costa Rica, the Dominican Republic, El Salvador, Guatemala, Honduras, Nicaragua and Panama had

reported altogether 32,961 cases of dengue, of which 500 were DHF.

In Mexico, the number of cases had reached 2,586 compared with 373 in the same period last year. Cases of DHF totalled 45 this year (12 deaths). In Brazil, 88,039 cases of classic dengue had been reported, including 105 cases of DHF. Some 57% of these cases come from the States of Rio de Janeiro, and from Bahia in the northeast. In Venezuela, 15,252 cases of dengue were reported this year, including 2,934 cases of DHF and 14 deaths.

In the English-speaking Caribbean, 228 cases of dengue fever have been reported since 1 January, 1995. The Caribbean Epidemiology Center has alerted its member countries to reinforce surveillance and mosquito control measures.

Dengue type 3 was recently detected in Nicaragua and Panama and, in early 1995, in Costa Rica, El Salvador, and Honduras - representing the reappearance of this strain in the Americas after an absence of 16 years.

The resurgence of dengue and emergence of DHF in the Americas is due in large part to setbacks in programs to eradicate the *Aedes aegypti* mosquito in the Region. Other causes leading to the reappearance of dengue include dramatic shifts in population,

population growth, more frequent international travel, and increasing poverty. Dengue is basically a problem of domestic sanitation. With little or no cost, members of each household can get rid of mosquito breeding areas by keeping water storage containers covered, removing or emptying other containers that can hold water, screening homes to keep the mosquito out, and killing mosquito larvae or adults.

Source: *WHO Weekly Epidemiological Record*, Vol 70, No 39, 1995.

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